I. The Office Action

The June 13, 2006 Final Office Action (the "Office Action") in this application:

1. rejected claims 22 and 26-29 under 35 U.S.C. 102(e);

2. rejected claims 22 and 25-29 under 35 U.S.C. 103(a);

3. rejected claims 22-29 under 35 U.S.C. 103(a); and

4. rejected claims 22 and 26-30 under 35 U.S.C. 103(a).

Applicant respectfully requests continued examination (RCE) and reconsideration of the pending claims in light of the amendments and comments provided below.

II. Amendment to claim 22 and new claim 36 and 37 and cancellation of claims 29-30

Support for the amendment "a transdermal patch, containing" botulinum toxin "provided in a dry state," in claim 22 can be found at least at page 19, lines 30-31 and page 27, lines 8-11 of the specification. Support for "applying a fluid to the patient's skin" and "solubilizing the botulinum toxin provided in the dry state by the fluid" can be found at least in the narrative at page 27, lines 16-19, as well as the method exemplified in Example 6, found on page 37 of the specification.

Support for new claim 36 can be found at least at page 27, lines 23-25 of the specification.

Support for new claim 37 can be found at least at page 30, lines 17-18 of the specification.

Claims 29 and 30 are hereby canceled without prejudice or disclaimer to prosecution at a later date.

III. Rejection of claims 22 and 26-29 under 35 U.S.C. 102(e)

The Office Action rejected claims 22 and 26-29 as being anticipated by Yuzhakov et al. Applicants respectfully traverse this rejection.

In accordance with MPEP 2131, a claim is only anticipated if each and every limitation/element is found, expressly or inherently, in a single reference. Solely and in order to facilitate prosecution, the claims are currently amended to include and define a particular aspect of one method for reducing neurotransmitter release in a subdermal structure of a patient, utilizing a transdermal patch that contains botulinum toxin provided in a dry state. Such a limitation cannot be found in Yuzhakov et al. Additional method steps recited in claim 22, where a fluid is applied to a patient's skin to which a transdermal patch, having the dry botulinum toxin, is applied in order to solubilize the dry botulinum toxin with the previously applied fluid, also cannot be found in Yuzhakov et al.

On another note, Applicant respectfully points out that is appears that the Office Action in its rejection has misconstrued the meaning of the term "polymers" in Yuzhakov et al. to mean an enhancing agent. A review of column 28 cited in the Office Action reveals that the term "polymers" (col. 28, line 63) is directed to and is part of a list of materials by which the "closed-loop system" and body-fluid sampling sensors, exemplified in Figures 30 and 31 of Yuzhakov et al., can be made of. The list of suitable material for construction of the "closed-loop system" includes diamond, bio-compatible metal, ceramics, polymers, polymer composites (col. 28, lines 60-65).

In this reference, botulinum toxin is mentioned in passing as part of a general list of "other types of skin structure modifiers can also be applied through the microneedle patch, including such ingredients as fat, collagen, botulinum toxin, fibril, silicones, hydrogels, elastomers, and colloids.", and certainly no distinction is made or provided by Yuzhakov et al. regarding providing botulinum

toxin in a dried state in a transdermal patch, nor discloses or suggests any advantages provided by a method that utilizes such an assembly, as disclosed by the instant specification. As each of the method steps and limitations recited in the pending claims cannot be found in Yuzhakov et al., it cannot anticipate the claims.

Thus, the rejection should be withdrawn.

III. Rejection of claims 22 and 25-29 under 35 U.S.C. 103(a)

The Office Action rejected claims 22 and 25-29 under 35 U.S.C. 103(a) as unpatentable over Yuzhakov et al. in view of Mitragotri et al. for reasons set forth on pages 4-6, paragraph 3 of the July 7, 2005 Office Action. Applicant respectfully traverses this rejection.

As detailed above, Yuzhakov et al. does not teach or even suggest a method in which reduction of neurotransmitter release in a subdermal structure of a patient is achieved by utilizing a transdermal patch that provides botulinum toxin in a dry state, nor does the Mitragotri et al. reference mention or suggest such a transdermal patch. Additionally, the step of applying a fluid onto a patient's skin, onto which the patch is placed in order to solubilize the dry botulinum toxin carried by the transdermal patch, is also not found in the Mitragotri et al. reference and thus the Mitragotri et al. disclosure does not remedy the deficiencies of Yuzhakov et al. The missing steps are only provided and found in the instant application and claims. Mitragotri et al. discloses ultrasound-mediated transdermal protein delivery, and does not mention transdermal patches, botulinum toxin or steps as presently detailed in the pending claims.

Thus, this rejection should be withdrawn.

IV. Rejection of claims 22-29 under 35 U.S.C. 103(a)

The Office Action rejected claims 22-29 under 35 U.S.C. 103(a) as unpatentable over Yuzhakov et al. in view of Mitragotri et al. and in further view of Smith et al. for reasons set forth on pages 6-7, paragraph 4 of the July 7, 2005 Office Action. Applicant respectfully traverses the rejection.

As detailed above, method steps such as applying a fluid to the patient's skin and applying a transdermal patch, containing botulinum toxin provided in a dry state, to the skin of the patient in an area that had had the stratum corneum disrupted, where the botulinum toxin provided in the dry state is subsequently solubilized by the fluid, are not found in Yuzhakov et al. or Mitragotri et al., alone or in combination. The addition of Smith et al. does not remedy these deficiencies, as no such steps are found therein. Furthermore, Smith et al. is directed to the use of tape stripping, which is *not* an abrasive method of disrupting the stratum corneum.

As Smith et al. does not remedy the missing steps and limitations currently recited in the pending claims and which are not found in either Yuzhakov et al. or Mitragotri et al., the addition of Smith et al. does not render any of the currently pending claims obvious.

Thus, this rejection should be withdrawn.

V. Rejection of claims 22 and 26-30 under 35 U.S.C 103(a)

The Office Action rejected claims 22 and 26-30 under 35 U.S.C 103(a) as being unpatentable over Yuzhakov et al. in view of Cevc et al. for reasons set forth on pages 7-8, paragraph 5 of the July 7, 2005 Office Action. Applicant respectfully traverses the rejection.

The Office Action asserts that Yuzhakov teaches various elements such as a microneedle array, a transdermal patch and botulinum toxin, enhancing agent (polymers), ultrasound to increase transdermal flow and application of electric potential across skin to increase permeability of the skin among other assertions. As stated above, there is no disclosure, either explicitly or implicitly, that can be found in Yuzhakov that relates to the use of a botulinum toxin in a dried state, in conjunction with a transdermal patch, as presently claimed. Additionally, there is no teaching or suggestion in the combination of Yuzhakov or Cevc that would suggest to one of ordinary skill in the art at least the currently recited step of applying a fluid to the patient's skin and applying a transdermal patch, containing botulinum toxin provided in a dry state, to the skin of the patient in an area that had had the stratum corneum disrupted in step, where the dry botulinum toxin is subsequently solubilized by the fluid.

Additionally, Cevc must be taken as a whole, and as such contrasts the use of its disclosed compounds with typical methods for administration of a drug, stating that its disclosed compounds do away with the need and use of needles to introduce a dosage of a compound to a patient (see col. 5 lines 7-21) and that "… dermally applied transfersomes can thus successfully replace injections of insulin solutions". Cevc also proceeds to disclose the shortcomings associated with injection needle usage to administer compounds and how the transfersomes are "…used for non-invasive applications of antidiabetic agents, most frequently insulin…" (col. 70, lines 3-50). This disclosure apparently teaches away from the use of compounds in Cevc in conjunction with needles and other

conventional skin disruption/transdermal methods, such as the microneedle array that is the subject of Yuzhakov and transdermal patches, and thus teaches away from combining the two disclosures.

Accordingly, an obviousness rejection is improper, since the cited references do not provide evidence to support the combinations made by the Office Action, but rather, such combinations are made in the face of contrary teachings in the references and at best raise a suggestion of what would be "obvious to try", which is not a proper standard (In re Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed.Cir.1988).

It is only by utilizing the instant specification and claims in an exercise of hindsight reconstruction can the disparate teachings of Cevc and Yuzhakov be combined to assert obviousness of the claims in light thereof.

Claim 30 has been deleted with out prejudice to further prosecution at a later date, and thus the instant rejection relating to transfersomes is moot, in addition to any rejection of the present claims in light of the improper combination of Yuzhakov et al. and Cevc.

Thus, this rejection should be withdrawn.